CAATAAAGTC CGGTACCACA ACGCGGCTTA ATTAAGGGCT AGGTCTGTAC TATTCTATGT AACTACTCAA ACCTGTTTGG TGTTGATCTT ACGTCACTTT ATAAGATACA TTGATGAGTT TGGACAAACC ACAACTAGAA 1 GITATITCAG GCCAIGGIGI IGCGCCGAAI IAAIICCCGA ICCAGACAIG

TGCAGTGAAA

- CTTCTGCAGG GAAGACGTCC TATTGCTTTA TITGTAACCA TTATAAGCTG CAATAAACAA GTTGGGCCAT GGCGGCCAAG (SEQ ID NO: 1)
- CCAGCTCGAA CCGCAGCACC GGTCGAGCTT GGCGTCGTGG æ PITTACGAAA TAAACACTIT AAACACTACG ATAACGAAAT AAACATTGGT AATATTCGAC GTTATTTGTT CAACCCGGTA CCGCCGGTTC TTACACACCC CTCAGAGAGC TGCCCCCGAG AGGATCCCCG GGGAATTCCG GCATGACTCG ATCGCCGCCC AAAATGCTTT 101
 - TAGCGGCGGG GAGTCTCTCG ACGGGGGCTC AATGTGTGGG ۲ × ഗ Д ជ ¢ Д Д W CGTACTGAGC M T R (SEQ ID NO: 2) TCCTAGGGGC CCCTTAAGGC insert starts here 201 TCGACTCTAG AGCTGAGATC
- GTAGAAGTGG GCTGGGAGCC TGAAGGCTCC ACTCTGGCTT CGTGCTTACT TCCAGGGCCT GCTCTTCTCT CYGGGATGCG GGATCCAGAG ACATTGTGGC TGTAACACCG Ø U ഗ L GCACGAATGA AGGTCCCGGA CGAGAAGAGA Ŋ Ľ Ц Н O Ø R A Y TGAGACCGAA **.** 3 ₽ CGACCCTCGG ACTTCCGAGG μ æ × O CCAGATCCTA GGTCTAGGAT 77
- CATCTTCACC CAGACCGCAC GCCAGGAGGG AAAGIGCTCT TICIGGGACT GITGGCCTTT GGGGCCCTGG CATTAGGTCT CCGCATGGCC AFTATTGAGA CAAACTTGGA ACAGCTCTGG Ø GTAATCCAGA GGCGTACCGG TAATAACTCT GTTTGAACCT z ۲ ជា I M A K G 1 H CCCCGGGACC ü e C TITCACGAGA AAGACCCTGA CAACCGGAAA Į, Ø H ပ > × 401
- CGGTCCTCCC CTGGGATTTG ធា GTCTGGCGTG ď Н 501 GCAGCCGGGT GAGCCAGGAG CTGCATTACA CCAAGGAGAA GCTGGGGGAG GAGGCTGCAT ACACCTCTCA GATGCTGATA H Σ Ø ഗ ⊱ E A A GACGTAATGT GGTTCCTCTT CGACCCCCTC [1] ပ Ļ, × ជា × ⊁ H CGTCGGCCCA CTCGGTCCTC 0 5
- ACCCCCCTCG GACCCTAAAC Ω 3 CTCACACCCG AAGCACTTGG CCTCCACCTC CAGGCAGCCC TCACTGCCAG TAAAGTCCAA GTATCACTCT ATGGGAAGTC × v ഗ GGAGGTGGAG GTCCGTCGGG AGTGACGGTC ATTTCAGGTT Ø X S Æ E A A L, I L GAGTGTGGGC TTCGTGAACC O N L ū Д AGAGAACATC TCTCTTGTAG 601
- GACCAACCTG GATCCAGAGC AGCTGCTGGA GCACTAGGAG TGGGGGGAGC 701 AACAAAATCT GCTACAAGTC AGGAGTTCCC CTTATTGAAA ATGGAATGAT TGAGTGGATG ATTGAGAAGC TGTTTCCGTG CGTGATCCTC Д [L TCCTCAAGGG GAATAACTTT TACCTTACTA ACTCACCTAC TAACTCTTCG M ſЦ Ι တ ŒΪ I I Q, > O CGATGTTCAG × >-TTGTTTAGA 157
- CTGGTTGGAC CTAGGTCTCG TCGACGACCT H 回 ρ, Ω Z AAACTCCAAG GGGGCTCCGC CTACCTGCCC GGCCGCCCGG ATATCCAGTG TITGAGGIIC CCCCGAGGCG GAIGGACGGG CCGGCGGGCC TAIAGGICAC × × ഗ O 0 X U GGAGGGAGCC CCTCCCTCGG O 801 ACTGCTTCTG TGACGAAGAC ្រ O

TCCCACAAAT CCGGGACAGA CCATGGCTTC GGGCCAGGCC TACGTGGGGC GGCCCTGTCT O Д CCCGGTCCGG ATGCACCCCG > × K Ø O GACGATCTGT TCCGTGTCCA CTTCCGGGAG CTGCTAGACA AGGCACAGGT > 0 Æ × Ω Ļ GAAGGCCCTC ĸ ſτι CCCTTTGCCT CCCTTGAGGG GGGAAACGGA GGGAACTCCC G ίτĵ ഗ ď (14 224

AGGGTGTTTA × Ħ GGTACCGAAG O Ħ CAATGIGGCT CACGAGCTGA GIGGGGGCTG CACCCCCGAC ပ ဖ O GTGCTCGACT ٦ H GTTACACCGA Æ > N GACCTCCACT GCCCACCTAG TGCCCCCAAC CATCACAGCA GGCAGGCTCC CCGTCCGAGG A P α GTAGTGTCGT ACGGGGGTTG CTGGAGGTGA CGGGTGGATC 1001

CAGAGCACCT TCTTGCTGAT AGAGGCCCTG S x Z ſ. U, 257

GTCTCGTGGA AGAACGACTA CAGTGCTACA AGCCTGGCAG ↵ ı, TCTCCGGGAC E A L GICTCIGGG GITCCICTCG ACGACTCCCG CAGAGACCCC CAAGGAGAGC TGCTGAGGGC R A H ជា O Ω æ GAGGCATGGC CTCCGTACCG Ø Σ (3) 1101 TCATGCACTG GCAGGAGGAA TTGCTGCTGG CGTCCTCCTT AACGACGACC <u>,</u> [1] 0 AGTACGTGAC 291

GTCACGATGT TCGGACCGTC O GTCCGGTCGT GAGTGAGGAG CTCACTCCTC ŧП ŧП ഗ CAGACACATG ACATTGGCTG GTCTGTGTAC TGTAACCGAC დ ლ Н Ω I E O CAGCIGIACG AGCATITCCG GGGIGACIAI CCCACTGATA ς Ω O TCGTAAAGGC (z. H GTCGACATGC CTCAGGGGCG GAGTCCCCGC 1201

CAGGCCAGCA

GACGTACGCA CTGCATGCGT GGATGACATC CCTACTGTAG CTGCCTGAGA ACGCTTCCCA GCAGATCCAT GCCTTCTCCT CCACCACCCT Y I O ഗ 324

GACTGCGCCC AGTCCCAGGG Д GACGGACTCT TGCGAAGGGT CGTCTAGGTA CGGAAGAGGA GGTGGTGGGA W A FI N I Q Ø S Ø Z ш 디 CCAGGAGGCC GGTCCTCCGG Ø ជា O CGCCCTTTG TGCAGCTGGC SCCGCGAAAC ACGTCGACCG L A 1301 357

CTGACGCGGG TCAGGGTCCC S ပ CGTGTGGTGG GAGGCTATCT GCTCATGCTG GCCTATGCCT GTGTGACCAT GCTGCGGTGG ж. Ж. +⊐ CTCCGATAGA CGAGTACGAC CGGATACGGA CACACTGGTA Σ T O A Y A L M L L × တ GCACACCACC O > × > 1401 TCTCTGAAGT CAGTGCTGCC AGAGACTTCA GTCACGACGG Ø æ ഗ 391

GAGCCGTAGT GGAAGTTACG CTCGGCATCA CCTTCAATGC CITACCEGEG TACTECTEGT GECCCTEGEG GTGGCCTCAG GCCTTGGGCT CTGTGCCCTG GACACGGGAC TTCCGTGGGC

CTCCAGGAGC Н r O Ø U CCGGGACCGC CACCGGAGTC CGGAACCCGA ↵ ഗ V A S Ø 'A L GAACGGCCCC ATGACGACCA ۲ ۲ AAGGCACCCG O 1501 424

GAGGTCCTCG TGGCACCCCT CGGAAGTGTC TCCGAGACGG ACCGTGGGGA Ö GCCTTCACAG AGGCTCTGCC A L P ₽ ſц Ø CITTCTTGGC TCTGGGAATC GCCGTGGATG ACGTATTCCT GCTGGCGCAT CCGCACCTAC TGCATAAGGA CGACCGCGTA X Ø ᇤ > Q ∧ 0 GTCCACGACG GAAAGAACCG AGACCCTTAG Н O ₊⊐ Ø 1601 CAGGTGCTGC ø 457

CACAGACGTC GCGTGCCCGT GGTCACAGCA TGAGTGTAGG TAGTTGTTGT ACCGGCGGAA GGAGTACCGA CGGGAGCAAG GGTAGGGACG GCCCTCGTTC CCATCCCTGC GIGTCTGCAG CGCACGGGCA CCAGTGTCGT ACTCACATCC ATCAACAACA TGGCCGCCTT CCTCATGGCT > O ۲ 0 ر, O CGTACCCGCT 1701 GCATGGGCGA

GGGACAGTAC CCTACGGCGG GGATGCCGCC æ Ļ CCAGCCATCC TCAGCCTGGA CGAACAGAAG GGTCGGTAGG AGTCGGACCT TGCACCTTTG TAGCCGTGAT GCTTGTCTTC 1 V F ACGTGGAAAC ATCGGCACTA A V M لتا Ę⊣ AGTGGTTGGC TCACCAACCG U Λ Λ TTCTCCCTAC AGGCGGCCAT AAGAGGGATG TCCGCCGGTA Ø CGACGCTCGG 1801 GCTGCGAGCC

AAGCCCACCT CCCTGTCATG 1901 COCCACTGCC AGCGCCTTGA TGTGCTCTGC TGCTTCTCCA GTCCCTGCTC TGCTCAGGTG ATTCAGATCC TGCCCCAGGA GCTGGGGGAC IQIL N Q K S U ρι ACACGAGACG ACGAAGAGGT ഗ ഗ EH, V L C GCGGTGACGG TCGCGGAACT Ω æ

GACGGAGGGG TTCGGGTGGA 2001 CAGIGGGCAT IGCCCACCTC ACTGCCACAG ITCAAGCCIT IACCCACTGI GAAGCCAGCA GCCAGCAIGI GGICACCAIC CIGCCICCC > ΝН Ø TGACGGIGTC AAGTICGGAA AIGGGIGACA CIICGGICGI ഗ E E O Ħ ĹĻ Ø Ø ۲ ۲ T A GTCACCCGTA ACGGGTGGAG I

591

GGCCAGGAGG AGGAGACAAG GCAGAAGGCA CGTCTTCCGT Ø CCGGTCCTCC TCCTCTGTTC ۲ ជា ជា α υ TGAGCTCTTC AGCCCTGGAG GGTCCACACG GGACCTTCTA CCTGGAAGAT H U L GGAAGACTGG GTGACCCGAG ACTCGAGAAG TCGGGACCTC CCAGGTGTGC ഗ ţı **,**_ ធា CCTTCTGACC CACTGGGCTC 2101 GGTGCCCCCA CCACGGGGGT

ACATGCCAAG GCCATCGTGC CGGTAGCACG GCCCCGTIGC TGCTCCAGTC ഗ O Ļ S D > 624

GACGGATGTG GTGCCTCGGG GCACCAAGGA TGTACGGTTC × Æ x CGGGGCAACG ACGAGGTCAG Ø P I 2201 GCCTGCAAGT CCCTGCCTG TGCCCGCTGG AATCTTGCCCC ATTTCGCCCG CTATCAGTTT TTAGAACGGG TAAAGCGGGC GATAGTCAAA [H > α Ø ជ NLAH ACGGGCGACC 3 æ CGGACGTTCA GGGACGGGAC U а

accacgagaa accacgagaa gacccggact cggagatgcc tcggtggaac cacgttctgc cggaccggga ctgcctacac cacggagccc cgtggttcct TGGTGCTCTT CTGGGCCTGA GCCTCTACGG AGCCACCTTG GTGCAAGACG GCCTGGCCCT ≻ ∵ C) Ļ ۱., 4 2301 TGGTGCTCTT

GCATGCCTTC CTGAGCGCCC AGCTCAGGTA CTTCTCCCTG TACGAGGTGG CCCTGGTGAC CCAGGGTGGC TTTGACTACG CCCATTCCCA ACGCGCCCTC TGCGCGGGAG **>**4 Ω ပ α CGTACGGAAG GACTCGCGGG TCGAGTCCAT GAAGAGGGAC ATGCTCCACC GGGACCACTG Ļ لتر R 2401

۲.,

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[14 Ø

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CGTGGGGCGT GGACCGACGT GATAATGGCG TTGACCGATG GCACCCCGCA CCTGGCTGCA CTATTACCGC * I H 3 pz, d K TTTGAICIGC ACCAGCGCTI CAGIICCCTC AAGGCGGTGC IGCCCCCACC GGCCACCAG TICCGCCACG ACGGGGGTGG CCGGTGGGTC ⊣ K ρų Д ρι K A V TGGTCGCGAA GTCAA.GGGAG တ S ſι pc, AAACTAGACG 2501

GCGCATCACC CGCCACTCGT ACCGCAATGG CTCTGAGGAT GGGGCCCTGG CCTACAAGCT CGCGTAGTGG GCGGTGAGCA TGGCGTTACC GAGACTCCTA CCCCGGGACC GGATGTTCGA & O Ω ш ഗ ഗ z ĸ E H GGCTGCCTTT GACCAGGACT GGGCTTCTGG CCGACGGAAA CTGGTCCTGA CCCGAAGACC ഗ Ø 3 (1, ⋖ A AGGGAATCCA TCCCTTAGGT Ω O [I4 2601

FIG. 10

CACGACAAAT GCTCGAGAAG CGAGCTCTTC GCTGGTGGAC AGAGAGGGAC TGALTCCACC TCTCTCCTG ACTAAGGTGG 瓦巴 CGACCACCTG Ω ر > CCCAGGAGCC TCTGGATTTC AGCCAGCTGA CCACAAGGAA TCGGTCGACT GGTGTTCCTT × ĸ ₽ H 0 ഗ GGGTCCTCGG AGACCTAAAG Ĺ Ω ы Ω, ជា GCTCATCCAG ACTGGAGACG SCACTAGGIC TGACCICTGC 824

GTGCTGTTTA CTGCAGACTT GACCCCCTGG GTCTGGCAGC CTCACAGGCC AACTTCTACC CCCCACCTCC TGAATGGCTG TTGAAGATGG GGGGTGGAGG ACTTACCGAC 3 Ω, Д ξĿι z CTGGGGGACC CAGACCGTCG GAGTGTCCGG 4 0 ഗ L A O H D, GGTGAGCAGT CCACTCGTCA ഗ ഗ > 2801 TACATGGGGC TGACCGTGTG ACTGGCACAC M A ATGTACCCCG Z >

GAGGTCTTCT GACGTCTGAA Д Ø CTCCAGAAGA CTTCGCATCC CGCCAGCTCA GCCCTTGGAG TTTGCCCAGT TCCCCTTCCT GCTGCGTGGC CGGGAACCTC AAACGGGTCA AGGGGAAGGA CGACGCACCG O æ ,ع Ľ٦٠ Д Ø E E •1 Θ D. GAAGCGTAGG GCGGTCGAGT Ø Ø <u>م</u> L R I CCCCCTCTTG GGGGGAGAAC z ĮП 2901 ACGACACCAC тестетете

891

CTGGGAACAG

TGGACGGCTG GACCCTTGTC ATCGAGGGGG CCCGGGCAGC ATGCGCAGAG GCCGGCCAGG CTGGGGTGCA CGCCTACCCC AGCGGCTCCC CCTTCCTCT 디 Œ O A Y P TAGCICCCC GGCCCCGICG TACGCGICTC CGGCCGGICC GACCCCACGI > ე 4 0 O A A U A ø, Ö ACACCTCCGG TGTGGAGGCC ſП 3001

ACCTGCCGAC GGAGTTGGGG TAICTGGGCC IGCGGCGCTG CTICCTGCTG GCCGICTGCA TCCTGCTGGT GTGCACTITC CTCGTCTGTG CTCTGCTGCT CCTCAACCCC r z CACGTGAAAG GAGCAGACAC GAGACGACGA U L V ۲ O ACGCCGCGAC GAAGGACGAC CGGCAGACGT AGGACGACCA L V ᄓ A V C ᆸ ᆸ **(**بر O œ ATAGACCCGG i i 3101

ATCCCCGTGG TGATCCTTGT TAGGGGCACC ACTAGGAACA > GCTGAGTGCC CGACTCACGG S Ļ GCCTCATAGT GCTGGTCCTG GCGATGATGA CAGTGGAACT CTTTGGTATC ATGGGTTTCC TGGGCATCAA CGCTACTACT GTCACCTTGA GAAACCATAG TACCCAAAGG ACCCGTAGTT H O 드 r S н ပ ſΞι ſΞÌ > A M M CGACCAGGAC ر د CGGAGTATCA 991

CGGAACCTGC GGGCCGCCCA TGCCCTTGAG GCCTTGGACG CCCGGCGGGT ACGGGAACTC **ب** ↵ Z Z GGCATTGGCG TIGAGTICAC AGTCCACGTG GCTCTGGGCT TCCTGACCAC CCAGGGCAGC AGGACTGGTG GGTCCCGTCG G Ø E E ü CCGTAACCGC AACTCAAGTG TCAGGTGCAC CGAGACCCGA > \square > £ ပ H C GGCCTCTGTA CCGGAGACAT 3301

CATTGTAAGG TACTTCTTTG GCTGGTTCCC ACTTTGACTT ഗ Ø

CGACCAAGGG TGAACTGAA GTAACATTCC ATGAAGAAAC ۲ ک Ω ſΞι I ഗ B G CACACATTTG CCCCCGTGAC CGATGGGGCC ATCTCCACAT TGCTGGGTCT GCTCATGCTT TAGAGGTGTA ACGACCCAGA CGAGTACGAA H r Z ი ე **,**, GGGGCACTG GCTACCCCGG R G Ω GTGTGTAAAC

AGTGCTCACG CTCCTGGGGCC TCCTCCATGG ACTCGTGCTG CTGCCTGTGC TGCTGTCCAT CCTGGGCCCG CCGCCAGAGG TGATACAGAT TCACGAGTGC GAGGACCCGG AGGAGGTACC TGAGCACGAC GACGGACACG ACGACAGGTA GGACCCGGGC GGCGGTCTCC ACTATGTCTA > م ۲ ۲ G L L H L L > CGGCGCTGAC GCCGCGACTG 3501

1091

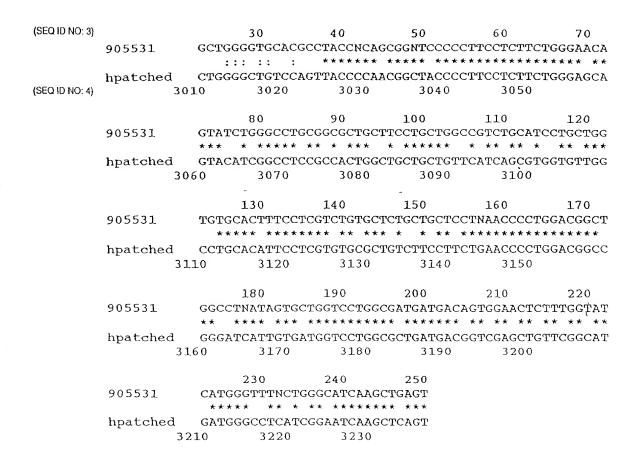
3701 ACTACCTCCA TGACCGTGGC CATCCACCCA CCCCCCTGC CTGGTGCCTA CATCCATCCA GCCCCTGATG AGCCCCCTTG GTCCCCTGCT GCCACTAGCT 3601 GTACAAGGAA AGCCCAGAGA TCCTGAGTCC ACCAGCTCCA CAGGGAGGCG GGCTTAGGTG GGGGGCATCO TCCTCCCTGC CCCAGAGCTT TGCCAGAGTG CATGITCCIT TCGGGTCTCT AGGACTCAGG TGGTCGAGGT GTCCCTCCGC CCGAATCCAC CCCCCGTAGG AGGAGGGACG GGGTCTCGAA ACGGTCTCAC TGATGGAGGT ACTGGCACCG GTAGGTGGGT GGGGGGGACG GACCACGGAT GTAGGTAGGT CGGGGACTAC TCGGGGGAAC CAGGGGACGA PPLPGAY L S P D,

3801 CTGGCANCCT CAGTTCCAGG GGACCAGGTC CAGCCACTGG GTGAAAGAGC AGCTGAAGCA CAGAGACCAT GTGTGGGGCG TGTGGGGTCA CTGGGAAGCA GACCGTTGGA GTCAAGGTCC CCTGGTCCAG GTCGGTGACC CACTTTCTCG TCGACTTCGT GTCTCTGGTA CACACCCCGC ACACCCCAGT GACCCTTCGT D D

3901 CTGGGTCTGG TGTTAGACGC AGGACGGACC CCTGGAGGGC CCTGCTGCTG CTGCATCCCC TCTCCCGACC CAGCTGTCAT GGGCCTCCCT GATATCGAAT GACCCAGACC ACAATCTGCG TCCTGC GGACCTCCCG GGACGACGAC GACGTAGGGG AGAGGGCTGG GTCGACAGTA CCCGGAGGGA CTATAGCTTA

of to C (silent)

AGITAGCTAT CTTGGCTCCA CGTCAACCTG 4001 TCAATCGATA GAACCGAGGT GCAGTTGGAC



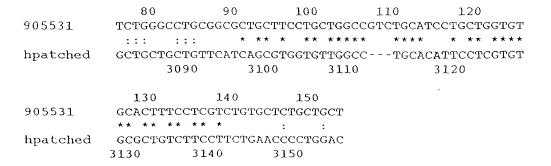
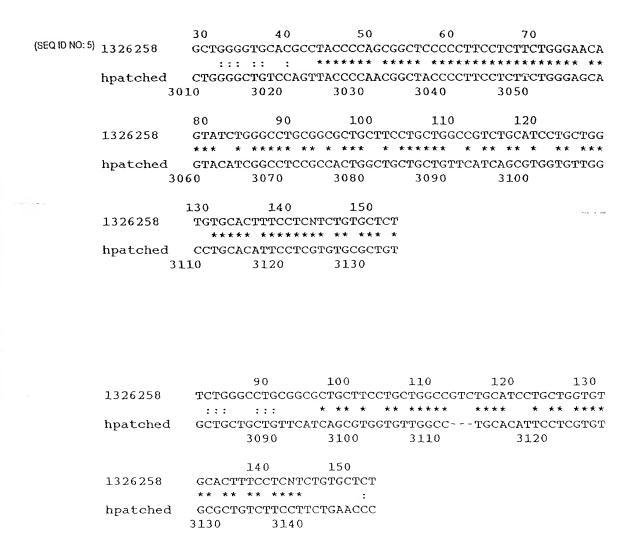


FIG. 2A



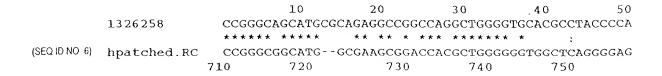


FIG. 2B

0 Y L E L . P P A Q RRRTGGLRRA MTR Œ α ഠ G A G (۵. Œ ഗ GCIGAP ഗ G മ QDRGG a. AGNAAE ഗ Υ (SEQ ID NO:2) PTCH2 SEQ ID NO:4) PTCH

1PSYCDAAFALEQISKGKATGRKAPLWLRAKFORLLFKLGCYIOKNGGK PSYTPP - - ARTAAPQILAGSLKAPLWLRAYFOGLLFSLGCGLORHCGK ۵ エ 51 PTCH2 FLVVGLL IFGAFAVGLKAANLETNVEELWVEVGGRVSRELNYTROKIGEE VLFLGLLAFGALALGLRMAIIETNLEOLWVEVGSRVSOELHYTKEKLGEE 101 PTCH2

AMFNPOLMIOTPKEEGANVLTTEALLOHLOSALOASRVHVYMYNROWKLE AAYTSQMLIOTAROEGENILTPEALGLHLOAALTASKVOVSLYGKSWDLN 151 PTCH2

(ପ ପ HLICYKSGELITETGYMDQIIEYLYPOLTITPLDCFWEGAKLOSGTAYLL Kicyksgvpliengmiewmieklfpcviiltplocfwegakloggsaylp 158 201 PTCH2

PLRWTNFDPLEFLEELKKINYQVDSWEEMINKAEVGHGYMDRPCLNPADIOWTNLDPEQLLEELGPFA.SLEGFREILLDKAQVGQAYVGRPCLHPD 자 R 다 이 PTCH2 PTCH

တ ဓ DPDCPATAPNKNSTKPLDMALVLNGGCHGLSRKYMHWQEELIVGGTVKN: DLHCPPSAPNHHSRQAPNVAHELSGGCHGFSHKFMHWQEELLLGGMARD 257 PTCH2

TIGKLVSAHALOTMFOLMTPKOMYEHFKGYEYIVSH.TNWNEDKAAAILEAW OGELLRAEALOSTFILLMSPROLYEHFRG.DYOTHDIGWSEEQASTVLOAW 351 PTCH2

IRTYVEVVHQSVAQNSTQKVLSFTTTTLDDILKSFSDVSVIRVASGYLLM RRFVQLAQEALPENASQQIHAFSSTTLDDILHAFSEVSAABVVGGYLLM 00 400 356

FIG. 3A

∀ ∀ TM3 LAYACLTMLRWDCSKSOGAVGLAGVLLVALSVAAGLGLCSLLGITFNA, LAYACVTMLRWDCAQSQGSVGLAGVLLVALAVASGLGLCALLGITFNA, PTCH2

TM4 LALGVGVDOVFLLAHAFSETGONKRIPFEDRTGECLKRTGASVA LALGIGVDOVFLLAHAFTEALPG..TPLQERMGECLQRTGTSVV TOVLPFL 456 PTCH2

S M D TM6
LTSTISMVTAFFMAAL IPIPALRAFSLOAA VVVVFNFAMVLLIFPAILE
LTSINNMAAFLMAAL VPIPALRAFSLOAA I VVGCTFVAVMLVFPAILE 504 PTCH2

တတ р У ı ഗ LYRREDRRLD | FCCF|TSPCVSRVIOVEPOAYTDTHONTRYSPPPPYS 554 009 PTCH2

ပ တ РАНЕТОІТМОЅТVОLЯПЕУОРНТНУУУПТАЕРЯЅЕІЅVОРУТУТОВТЦЅ! PTCH2

പഗ) SPESTSSTRDLLSOFSDSSLH - - OLEPPOTKWTLSSFAEKHYAPFLLK F LFSPGGSTRDLLGOEEETROKAACKSLPOARWNLAHFARYOFAPLLLOS oш 700 634 PTCH2

TM7

*** KAKN VVVI FLFLGLLGVSLYGTTRVRDGLDLTD I VPRETTREYDFI AAOFKY

**** HAKA IVLVLEGALLLGLSLYGATLLVODGLALTDVVPRGTKEHAFLSAOLRY PTCH2

SFYNMY IVTOKA - DYPNIOHLLYDL HRSFSNVKYVM LEENKOLPKMWL H SLYEVALVTOGGFDYAHSORALFDLHORFSSLKAVLPPPATOAPRTWLH

FIG. 3B

م م ᆇᇤ YFRDWLQGLQDAFDSDWETGKTMPNNYKNGSDDGVLAYKLLVQTGSRDI YYRNWLQGIQAAFDQDWASGRLTRHSYRNGSEDGALAYKLLIQTGDAQ1 PTCH2

0 ID ISOLTKORLVDADGIINPSAFYIYLTAWVSNDPVAYAASOANIRPHRF LDFSOLTTRKLVDREGLIIPPELFYMGLTVWVSSDPLGLAASOANFYPPPE PTCH PTCH2

<u>E</u> E EWVHDKADYMPETRLRIPAAEPIEYAOFPFYLNGLRDTSOFVEAIEKVIEWLHDKYD) TTGENLRIPPAOPLEFAOFPFLLRGLOKTADFVEAIEGAL

947

TM8
FLFWEQY | GLRHWLLTF1SVVTACTFLVCALF SSYPNGYPF AAYPSGSPF A C A E A G Q A G V H / PTCH2

TL L G V E TM9

TM9

TM9

LENPWTAG 1 IVMVLALMTVELFG MMGL 1 G 1 K LSA VP VV 1 L 1 A S V G 1 I L L N P W T A G L L V L A MM T V E L F G 1 M G F L G 1 K L S A 1 P V V 1 L V A S V G 1 I

ட ட шІ လ လ ග ග TM11
1097 TVHVALAFLTA IGDKNRRAVLALEHMFAPVLDGAVSTLLGVLMLA(
1033 TVHVALGFLTTOGSRNLRAAHALEHTFAPVTDGA ISTLLGLEMLA(PTCH 1097

മഗ ப ப α л ж п п п EVSPANC F F G P Y P E TM12 FIVRYFFAVLAJLTHEGVLNGLVLLPVLLSF FIVRYFFAALTVLTLLGLLHGLVLLPVLLS

വ പ ∢ ₽ ٩ EL BHY шо SOTTVSGLSE /AIHPPPLPG S M T V A PPSVVRFAMPPGHTHSGSDSSDS QGGGLRWGASSSLPQS-FARVTT <u>а</u> а ام ما ഗെ 1133

PTCH 1247 AGGPAHQVIVEATENPVFAHSTVVHPESRHHPPSNPRQQPHLDSGSLPP(PTCH2 1182 PWSPAATSSGNLSSRGPGPATG

ഗ

PTCH 1297 ROGOOPRRDPPREGLWPPLYRPRRDAFEISTEGHSGPSNRARWGPRGARS

PTCH 1347 HNPRNPASTAMGSSVPGYCQPITTVTASASVTVAVHPPPVPGPGRNPRGG

PTCH 1397 LCPGYPETDHGLFEDPHVPFHVRCERRDSKVEVIELQDVECEERPRGSSS

PTCH 1447 N

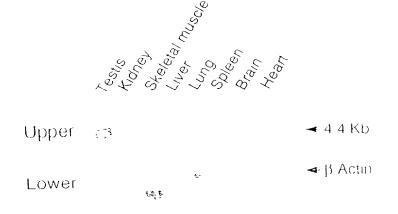


FIG. 4

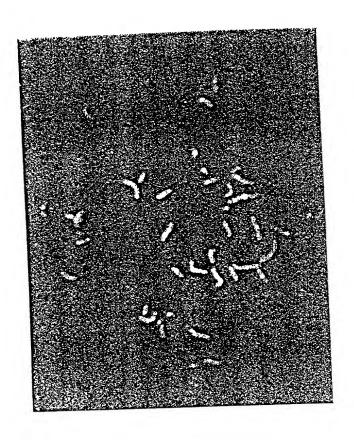
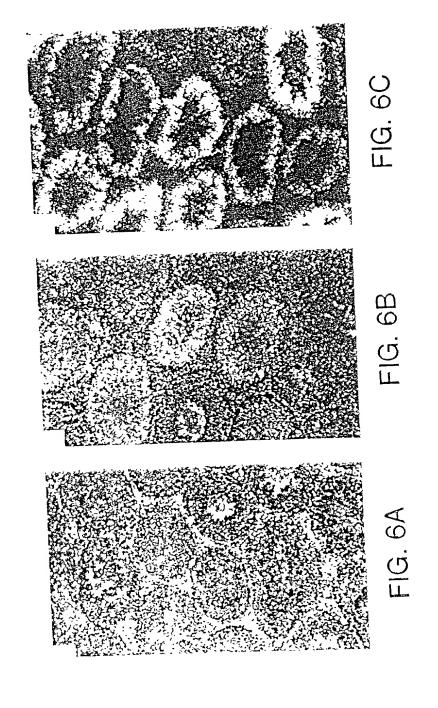
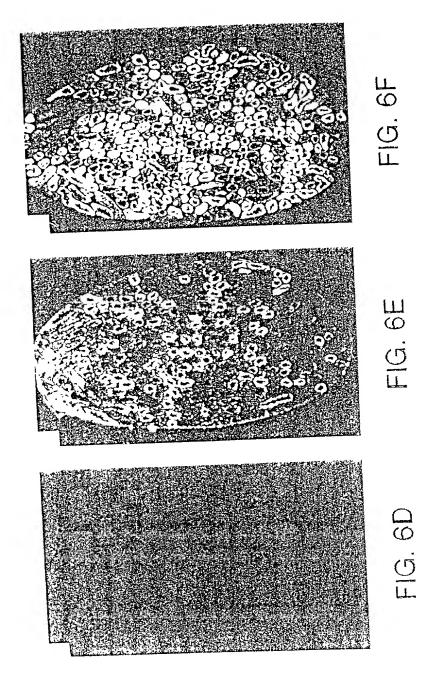
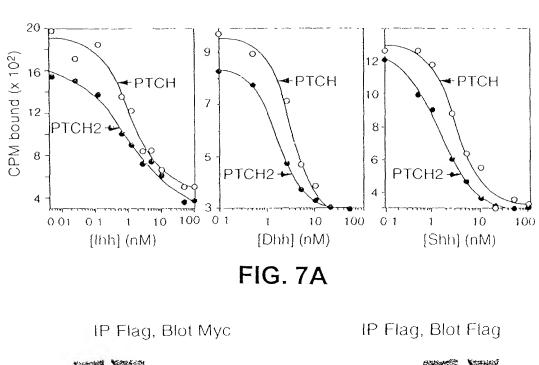


FIG. 5







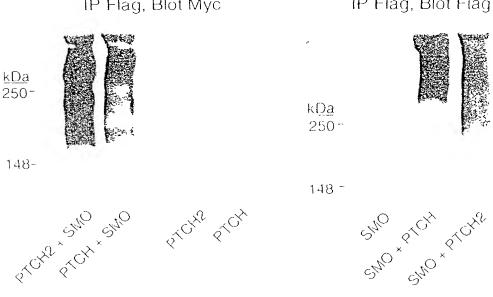


FIG. 7B

h <i>Ptch-</i> 2	MTRSPPLRE			30 AGSLKAPLWLR		
mPatched2 (SEQIDNO:7)		LPPSYTPP 10	ARSSAPHILA 20	AGSLQAPLWLR 30	AYFQGLLFSL 40	GCR 50
h <i>Ptch-</i> 2	IQRHCGKVI			80 IETNLEQLWV ***		
mPatched2	· -	FLGLVAFG 0	ALALGLRVA\ 70	/IETDLEQLWV 80	EVGSRVSQEL 90	НҮТ 100
h <i>Ptch-</i> 2	*****	YTSQMLIQ'	**.*** *.*	130 TPEALGLHLQ ***** TPEALDLHLQ	****	***
mr acchedz	11	LO	120	130	140	150
h <i>Ptch</i> -2		CYKSGVPL		180 [EKLFPCVIL] ******		
mPatched2	GKSWDLNK	CYKSGVPL		IEKLFPCVILI 180		
h <i>Ptch-</i> 2 mPatched2	GSAYLPGRI ******* GSAYLPGRI	PDIQWTNLD ******* PDIQWTNLD	* . * * * * * * * *	230 PFASLEGFREI ******** PFASLEGFREI 230	******	***
h <i>Ptch-</i> 2 mPatched2	20 PCLHPDDLI	50 HCPPSAPNH ******	270 HSRQAPNVAI ******	280 HELSGGCHGFS .***********	290 SHKFMHWQEEI	300 LLLG ****
mracchedz	2	60	270	280	290	300
h <i>Ptch</i> -2	GMARDPQG:	ELLRAEALQ		330 QLYEHFRGDY(******		
mPatched2		QLLRAEALQ 10	STFLLMSPRO	QLYEHFRGDY(330	OTHDIGWSEE(340	2ASM 350

FIG. 8A

h <i>Ptch-</i> 2			380 SQQIHAFSSTTLI				
	*****	*****	*****	****	****		
mPatched2	VLQAWQRRFVQ!	LAQEALPANAS	EQQIHAFSSTTL	DDILRAFSEVS	STTRVVG		
	360	370	380	390	400		
t. D. J. O	410	420	430	440	450		
h <i>Ptch</i> -2			QGSVGLAGVLLV				

mPatched2	GYLLMLAYACV'	TMLRWDCAQS(QGAVGLAGVLLV	ALAVASGLGLO	CALLGIT		
	410	420	430	440	450		
	460	470	480	490	500		
h <i>Ptch-</i> 2			FLLAHAFTEALP				
			*****		-		
mPatched2	FNAATTQVLPF	LALGIGVDDII	FLLAHAFTKAPP	DTPLPERMGEO	LRSTGT		
	460	470	480	490	500		
	510	520	530	540	550		
h <i>Ptch-</i> 2			PALRAFSLQAAI				
	** ***.*** **.************* * * *******						
mPatched2	SVALTSVNNMV.	AFFMAALVPII	PALRAFSLQAAI	VVGCNFAAVMI	VFPAIL		
	510	520	530	540	550		
	560	570	580	590	600		
h <i>Ptch-</i> 2			CSAQVIQILPQE				
	******* **********************						
mPatched2	SLDLRRRHRQR	LDVLCCFSSP	CSAQVIQMLPQE	LGDRAVPVGI <i>H</i>	HLTATV		
	560	570	580	590	600		
	610	620	630	640	650		
h <i>Ptch</i> -2	~ ~		HLVPPPSDPLGS				
			.	-	=		
mPatched2	QAFTHCEASSQ	HVVTILPPQAI	HLLSPASDPLGS	ELYSPGGSTRI	OLLSQEE		
	610	620	630	640	650		
	660	670	680	690-	700		
h <i>Ptch-</i> 2			ARYQFAPLLLQS				

mPatched2	GTGPQAACRPL	LCAHWTLAHF.	ARYQFAPLLLQT	RAKALVLLFF	GALLGLS		
	660	670	680	690	700		

FIG. 8B

h <i>Ptch-</i> 2	710 LYGATLVQDGLALTD ********* LYGATLVQDGLALTD	*****	*****	*****	*****
	710	720	730	740	750
hPtch-2	760 HSQRALFDLHQRFSS ********				
mPatched2	HSQRALFDLHQRFSS 760	LKAVLPPPA 770	TQAPRTWLHY 780	YYRSWLQGIQA 790	AFDQDW 800
h <i>Ptch-</i> 2	810 ASGRITRHSYRNGSE ***** ******			-	
mPatched2	ASGRITCHSYRNGSE 810				
h <i>Ptch-</i> 2	860 IPPELFYMGLTVWVS ******		· -		
mPatched2	IPPELFYMGLTVWVS				
h <i>Ptch-</i> 2	910 PAQPLEFAQFPFLLR .*********				
mPatched2	AAQPLEFAQFPFLLH				
h <i>Ptch-</i> 2	960 FLFWEQYLGLRRCFI ******				
mPatched2	FLFWEQYLGLRRCFI 960			-	
h <i>Ptch-</i> 2	1010 VELFGIMGFLGIKLS ******			-	-
mPatched2	VELFGIMGFLGIKLS				

FIG. 8C

GL **					
* *					
GL					
00					
50					
LP					
* *					
LP					
50					
00					
QSFARVTTSMTVAIHPPPLPGAYIHPAPDEPPWSPAATSSGNLSSRGPGP					

QSFARVTTSMTVALHPPPLPGAYVHPASEEPT					

FIG. 8D

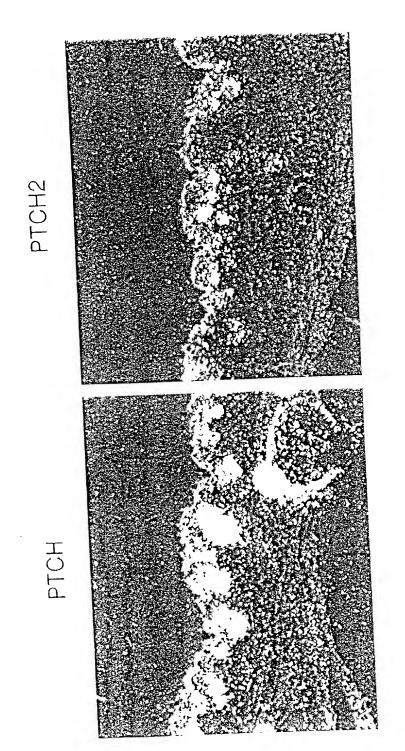


FIG. 9

Consensus Sequence of human patched 2 cDNA clone

> length: 4004 bp

(SEQ ID NO:8)

1 CCCACGCGTC CGGGAGAAGC TGGGGGAGGA GGCTGCATAC ACCTCTCAGA TGCTGATACA GACCGCACGC CAGGAGGGAG AGAACATCCT CACACCCGAA GGGTGCGCAG GCCTTTTCG ACCCCTCCT CCGACGTATG TGGAGAGTCT ACGACTATGT CTGGCGTGCG GTCCTCCCTC TCTTGTAGGA GTGTGGGCTT

race 5' 101 GCACTINGGCC TCCACCTCCA GGCAGCCCTC ACTGCCAGTA AAGTCCAAGT ATCACTCTAT GGGAAGTCCT GGGATTIGAA CAAAATCTGC TACAAGTCAG CGTGAACCGG AGGTGGAGGT CCGTCGGGAG TGACGGTCAT TTCAGGTTCA TAGTGAGATA CCCTTCAGGA CCCTAAACTT GTT<u>TTAGACG ATGTTCAGTC</u>

201 GAGITICCCCT TAITGAAAAI GGAATGAITG AGCGGATGAT TGAGAAGCTG TITICCGTGCG TGATCCTCAC CCCCCTCGAC TGCTTCTGGG AGGGAGCCAA CTCAAGGGGA ATAACTTTTA CCTTACTAAC TCGCCTACTA ACTCTTCGAC AAAGGCACGC ACTAGGAGTG GGGGGAGCTG ACGAAGACCC TCCCTCGGTT

TGAGGITCCC CCGAGGCGGA TGGACGGCGA GGGITACACC GAGTGCTCGA CTCACCCCG ACGGTACCGA AGAGGGTGIT TAAGTACGTG ACCGTCCTCC ACTECAAGGG GGETEEGEET ACCTGEEGET ECCAATGIGG ETEAEGAGET GAGIGGGGG IGECAIGGET IETECEGAAA ATTEAIGEAE IGGEAGGAGG 301

AATTICTICT GGGAGGCATG GCCAGAGACC CCCAAGGAGA GCTGCTGAGG GCAGAGGCCC TGCAGAGCAC CTTCTTGCTG ATGAGTCCCC GCCAGCTGTA TTAACGACGA CCCTCCGTAC CGGTCTTCGG GGGTTCCTCT CGACGACTCC CGTCTCCGGG ACGTCTCGTG GAAGAACGAC TACTCAGGGG CGGTCGACAT 401

501 CGAGCATTIC CGGGGTGACT ATCAGACACA TGACATIGGC TGGAGTGAGG AGCAGGCCAG CACAGTGCTA CAAGCCTGGC AGCGGCGCTT TGTGCAGGTC GCTCGTAAAG GCCCCACTGA TAGICTGTGT ACTGTAACCG ACCTCACTCC TCGTCCGGTC GTGTCACGAT GTTCGGACCG TCGCCGCGAA ACACGTCCAG

GGIAIGGACA AGGACAGGGG GGIGCCCIGA GGCCAITICCC ICCICCIGCC CCCICCIAIC CACCCIGITY CICCAGCIGG CCCAGGAGGC CCIGCCIGAG CCATACCTGT TCCTGTCCCC CCACGGGACT CCGGTAAGGG AGGAGGACGG GGGAGGATAG GTGGGACAAA GAGGTCGACC GGGTCCTCCG GGACGGACTC 601

701 AACGCTTCCC AGCAGATCCA TGCCTTCTCC TCCACCACCC TGGATGACAT CCTGCATGCG TTCTCTGAAG TCAGTGCTGC CCGTGTGGTG GGAGGCTATC TTGCGAAGGG TCGTCTAGGT ACGGAAGAGG AGGTGGTGGG ACCTACTGTA GGACGTACGC AAGAGACTTC ARTCACGACG GGCACACCAC CCTCCGATAG

CCCCACAGCT

ACGAGTACCA CCCAGAACGT GGACCGTGGA ACGGGGGTGG GGTGGAGGTT GGTCACGGGT GGGACCCCTC GGGGACTCTG ACGGGAAAGG GGGGTGTCGA IGCTCAIGGI GGGICTIGCA CCIGGCACCI IGCCCCCACC CCACCICCAA CCAGIGCCCA CCCIGGGGAG CCCCIGAGAC IGCCCTITICC 801

FIG. 10A

23 į.

- COGGATACGG ACACACTGGT ACGACGCCAC CCTGACGCGG GTCAGGGTCC CAAGGCACCC GGAACGGCCC CATGACGACC ACCGGGACCG CCACCGGAGT GGTGGCCTCA recreceere edacrecece cagreceage errecerese cerrecesse gracrecres resectings GGCCTATGCC 901
 - ACCITICAATG CIGCCACIAC CCAGGIACGC CAGGACTGCA GGGCAGACIC AGIGCCAGIC ACCAGGCITIC CCGGAACCCG AGACACGGGA CGAGCCGTAG TGGAAGTTAC GACGGTGATG GGTCCATGCG GTCCTGACGT CCCGTCTGAG TCACGGTCAG TGGTCCGAAG gecerreged rerereceer 1001
- TGCCCAGGAG TCGACGGGCG AGGAGGCGGG GAGGTCCACG ACGGGAAGAA CTGAGACCTT TAGCCGCACC TACTGCATAA GGACGACCGC GTACGGAAGT GGTTCAAGTG GACTCTGGGA ATCGGCGTGG ATGACGTATT CCTGCTGGCG ACGGGTCCTC AGCTGCCGG TCCTCTGCCC CTCCAGGTGC TGCCCTTCTT 1101

CATGCCTTCA

- ATCAGTGAAG GTCTCCGAGA CGGACCGTGG GGAGAGGTCC ACCCGGAAC AGGGGGTCCC GAGTAGACTC CGTCGAGTCG AATGACCAAT TCTCGGAGAA CCAAGTTCAC CAGAGGCTCT GCCTGGCACC CCTCTCCAGG TGGGGCCTTG TCCCCCAGGG CTCATCTGAG GCAGCTCAGC TTACTGGTTA AGAGCCTCTT 1201
- TGGAACCCGA CGAITACTTG GAGCCACGGA GAACAGGGGI ACACATTTGT CCCCTTTATT ATCACGACAC AGGATTCCCA ATAACAAACC TAGTCACTTC GCTAATGAAC CTCGGTGCCT CTTGTCCCCA TGTGTAAACA GGGGAAATAA TAGTGCTGTG TCCTAAGGGT TATTGTTTGG ACCTTGGGCT 1301
 - TGAATGCITA GAACAGCCCA TCATACGTAC ATGGTACCCA ATAAATGCTA GCCACTGTGT TATGACTGCC CCACCTCTGC ACCCCAAGIT ATTGAGTTCA ACTTACGAAT CTTGTCGGGT AGTATGCATG TACCATGGGT TATTTACGAT CGGTGACACA ATACTGACGG GGTGGAGACG TAACTCAAGT 1401
- COGCCCCTCC CTTGTGACCT GAGGGCAGGT CCCCACTCTG TCCTGGCAGG AGCGCATGGG CGAGTGTCTG GGACTCGGAG GGGAAGTGAG GTGAAACTGT GCCGGGGAGG GAACACTGGA CTCCCGTCCA GGGGTGAGAC AGGACCGTCC TCGCGTACCC GCTCACAGAC CCTGAGCCTC CCCTTCACTC CACTTTGACA 1501
 - GTCGCGTGCC CGTGGTCACA ACATGAGTGT AGGTAGTTGT TGTACCGGCG GAAGGAGTAC CGACGGGAGC AAGGGTAGGG ACGCGACGCT CGGAAGAGGG CAGCGCACGG GCACCAGTGT TGTACTCACA TOCATCAACA ACATGGCCGC CTTCCTCATG GCTGCCCTCG TTCCCATCCC TGCGCTGCGA GCCTTCTCCC 1601
- ATGTOGGACO TOGATGOOGO COOGGTGACG GTOGOGGAAC TACACGAGAC GACGAAGAGG TOCATGACGG ACGOGGGGTO GGGGAAGGAG GGCACTGGGT receccede cecerrecte cestances TACAGCCTGG ACCTACGGCG GCGCCACTGC CAGCGCCTTG ATGTGCTCTG CTGCTTCTCC AGGTACTGCC 1701
- CECCAGCCIG ICCCCICACC AGCATITCAA GGCACAGACC IGTCAICCAC ICTCIACCIC IICCAGICCC IGCICIGGIC AGGIGALICA 1801
 - GEGACGEGAC AGTACCAGTG GGCATTGCCC ACCTCACTGC CACAGTTCAA GCCTTTACCC ACTGTGAAGC CAGCAGCCAG CATGTGGTCA COUTGOOCTE TOATGGTOAC COGTAACGGG TGGAGTGACG GTGTCAAGTT CGGAAATGGG TGACACTTCG GTCGTCGGTC GTACACCAGT GTCCTCGACC CAGGAGCTGG 1901
 - COCCACCITO TGACCCACTG GGCTCTGAGC TCTTCAGCCC TGGAGGGTCC ACACGGGACC TTCTAGGCCA GGTAGGACGG AGGGGTTCGG GTGGACCACG GGGGTGGAAG ACTGGGTGAC CCGAGACTCG AGAAGTCGGG ACCTCCCAGG TGTGCCCTGG AAGATCCGGT CCATCCTGCC TCCCCAAGCC CACCTGGTGC 2001

- 2101 GGAGGAGGAG ACAAGGCAGA AGGCAGCCTG CAAGTCCCTG CCCTGTGCCC GCTGGAATCT TGCCCATTTC GCCCGCTATC AGTTTGCCCC GTTGCTGCTC COTOCTOCTO TGITTCOGICT TOOGTOGGAC GTTCAGGGAC GGGACACGGG CGACOTTAGA ACGGGTAAAG CGGGCGATAG TCAAACGGGG CAACGACGAG
- STCAGIGIAC GGIICCGGIA GCACGACCAC GAGAAGCCAC GAGAAGACCC GGACTCGGAG AIGCCICGGI GGAACCACGI ICIGCCGGAC CGGGACTGCC CAGICACAIG CCAAGGCCAI CGIGCIGGIG CICITIGGIG CICTICIGGG CCIGAGCCIC IACGGAGCCA CCIIGGIGCA AGACGGCCIG 2201

GCCCTGACGG

- TACACCACGG AGCCCCGTGG TICCTCGTAC GGAAGGACTC GCGGGTCGAG TCCATGAAGA GGGACATGCT CCACCGGGAC CACTGGGTCC CACCGAAACT CCCTGTACGA GGTGGCCCTG GTGACCCAGG GTGGCTTTGA ATGTGGTGCC TCGGGGCACC AAGGAGCATG CCTTCCTGAG CGCCCAGCTC AGGTACTTCT 2301
- GATGCGGGTG AGGGTTGCGC GGGAGAAAT AGACGTGGTC GCGAAGTCAA GGGAGTTCCG CCACGACGGG GGTGGCCGGT GGGTCCGTGG GGCGTGGAACC CCACCGGCCA CCCAGGCACC CCGCACCTGG CTACGCCCAC TCCCAACGCG CCTCTTTGA TCTGCACCAG CGCTTCAGTT CCCTCAAGGC GGTGCTGCCC 2401
- GACGIGATAA TOGCGTIGAC CGAIGICCCI IAGGICCGAC GGAAACIGGI CCIGACCCGA AGACCCGCGI AGIGGGCGGI GAGCAIGGCG ITACCGAGAC CTGCACTATT ACCGCAACTG GCTACAGGGA ATCCAGGCTG CCTTTGACCA GGACTGGGCT TCTGGGCGCA TCACCCGCCA CTCGTACCGC AATGGCTCTG 2501
 - CCTGGCCTAC AAGCTGCTCA TCCAGACTGG AGACGCCCCAG GAGCCTCTGG ATTTCAGCCA GGTTGGGAGA GGGCTGGAGG GGTCCACTAG rectaecece geacegeate tresagaast aggretsace tetgegggte etegagaee taaagteggt ecaaecetet eegaeetee ceaggigate AGGATGGGGC 2601
- ATGTCCCCGA CGTCCGGAGG ACCCGGGTCC GGAGTCGGG AGAGACGGAG ACGTCGACTG GTGTTCCTTC GACCACCTGT CTCTCCTGA CTAAGGTGGG 2701 TACAGGGGCT GCAGGCCTCC TGGGCCCAGG CCTTCAGCCC TCTCTGCCTC TGCAGCTGAC CACAAGGAAG CTGGTGGACA GAGAGGGACT GATTCCACCC GAATGGCTGC
- CTTACCGACG GAGCTCTICT ACATGGGGCT GACCGTGTGG GTGAGCAGTG ACCCCCTGGG TCTGGCAGCC TCACAGGCCA ACTTCTACCC CCCACCTCCT CTCGAGAAGA TGTACCCCGA CTGGCACACC CACTCGTCAC TGGGGGACCC AGACCGTCGG AGTGTCCGGT TGAAGATGGG GGGTGGAGGA 2801
 - 2901 ACGACAAATA CGACACCACG GGGGAGAACC TTCGCAGTGA GTCTTGGGGG GAGCTCGGCA AGAGCCTCAG CCTCGCCCAC ACAAGCCCTG AGCCTGAGGC rectental ecteregree eceptoring areceteat cagaaceee etegageegt reteggagie ggagegggtg tettegggae icggaactees AGTTTGCCCA CONGECEARY ENGRECEGENG ENCACEGENE TONDECTION CONTENTE CONTECTOR CONTENTED CONTEGER CONTEGER CONTENTS CONTEGER CONTENTS C

GGACGGGTGA GACGGGGACAC GAGTGGCGGG ACAGGGAGAG GGAGAAGAGG GAAGGGGAGG GGAGGTGTCA GGGCGGTCGA GTCGGGAACC TCAAACGGGT

3001

3101 GITCCCCTIC CIGCIGCGIG GCCTCCAGAA GACIGCAGAC ITIGIGGAGG CCATCGAGGG GGCCCGGGCA GCAIGCGCAG AGGCCGGCCA GGCTGGGGIG CAAGGGGAAG GACGACGCAC CGGAGGTCTT CTGACGTCTG AAACACCTCC GGTAGCTCCC CCGGGCCGGT CGTACGCGTC TCCGGCCGGT CCGACCCCAC TGGCCGTCTG CATCCTGCTG GTGTGCACTT GTGCGGATGG GGTCGCCGAG GGGGAAGGAG AAGACCCTTG TCATAGACCC GGACGCCGCG ACGAAGGACG ACCGGCAGAC GTAGGACGAC CACACGTGAA CCCTTCCTC TICTGGGAAC AGTAICTGGG CCTGCGGCGC TGCTICCTGC CCAGCGGCTC CACGCCTACC 3201

GGACCTGCCG ACCGGAGTAT CACTCACGAA CGTCCTCACC CCTGTCTCTG TGGGGTGGGA AGGGACGGGT TCCCTGCCCA CCTGGACGGC TGGCCTCATA GTGAGTGCTT GCAGGAGTGG GGACAGAGAC ACCCCACCCT AGGAGCAGAC ACGAGACGAC GAGGAGTTGG CTCCTCAACC TCCTCGTCTG TGCTCTGCTG 3301

cgalcagtag ggaggalggt coticgggaga caltigggal agagggagte calgalcagg accgetacta etgteacett gagaaaceat agtacecaaa TGGCGATGAT GACAGTGGAA CTCTTTGGTA TCATGGGTTT GTGCTGGTCC GCCTGTCATC CCTCCTGCCA GGAGCCCTCT GTGAGCCCTG TCTCCCTCAG 3401

GGACCCGTAG TICGACTCAC GGTAGGGGCA CCACTAGGAA CACCGGAGAC ATCCGTAACC GCAACTCAAG IGTCAGGTGC ACCGAGACCA CTCGTGCCCG COTGGGCATO AAGOTGAGTG COATCCCCGT GGTGATCCTT GTGGCCTCTG TAGGCATTGG CGTTGAGTTC ACAGTCCACG TGGCTCTGGT GAGCACGGGC

3501

ACCCCGGGGA GGGACCAATC AGCTGATTCA GTATTCAACA CATATTGTTC AAGCCCCTAC TATGTGCTAG GTACTATTTA AGAATTTGGG CTGGGTGGAC rggggccct cctggttag tcgactaagt cataagttgt gtataacaag ttcggggatg atacacgatc catgataaat tcttaaaccc gacccacctg 3601

GIGGISGCIC AIICCIGIAA ICCCAGCACI IIGGGAGGCC GAGGCGGGIG GAICACCIGA GGICGGGAGI ICGAAACCAG CCIGGCCAAC AIGGIGAAAC CACCACCGAG TAAGGACAIT AGGGICGIGA AACCCICCGG CICCGCCCAC CIAGIGGACI CCAGCCCICA AGCITIGGIC GGACCGGIIG TACCACIIIG 3701

CTCCGACTCC GTCTTAACGA ACTTGGACCC TGAACCTGGG AAAAATTAG CCAGGCGTGG TGGCACATGC CAGTAGTCCC AGCTACTTTG GAGGCTGAGG CAGAATTGCT GGACAGAAAT GAITTITATG ITTITIAATC GGICCGCACC ACCGIGIACG GICATCAGGG TCGAIGAAAC CCTGTCTTTA CTAAAAATAC 3801

AGGCGAAGGT TGCAGTGAGC TGAGATCGTG CCATTGCACT CCAGCCTGGG CAACAAGAGT GCAACTCTCC GTCTCAAAAA AAAAAAAA AAGGGCGGCC PCCGCTTCCA ACGTCACTCG ACTCTAGCAC GGTAACGTGA GGTCGGACCC GTTGTTCTCA CGTTGAGAGG CAGAGTTTTT TTTTTTTT TTCCCGCCGG 3901

4001 GCGA

CGCT

FIG. 10D

Clone 16.1 human patched > length: 2082 bp

N

(SEQ ID NO:9)

- renceacede secreaater stessestes acertesest estessester assarcaace eressaerre GAGCCTGAAG TCCTAGCTGG TICCOGÉATG ACTOGATOGO COCCOTOAG AGAGOTGOCO COGAGITACA CACCOCOAGO TOGAACOGOA GCACOCOAGA AAGGECGTAC TGAGCTAGCG GCGGGAGTC
 - CGAGGTGAGA CCGAAGCACG AATGAAGGTC CCGGACGAGA AGAGAGCCC TACGCCCTAG GTCTCTGTAA CACCGTTTCA CGAGAAAGAC CCTGACAACC GCTCTTTCTG GGACTGTTGG GTGGCAAAGT CAGAGACATT GGCCTGCTCT TCTCTGGG ATGCGGGATC 101 GCTCCACTCT
- AGGAGCTGCA GCCCACTCGG TCCTCGACGT CGGGTGAGCC GGAAACCCCG GGACCGTAAT CCAGAGGCGT ACCGGTAATA ACTCTGTTTG AACCTTGTCG AGACCCATCT TCACCCGTCG TGGCCATTAT TGAGACAAC TTGGAACAGC TCTGGGTAGA AGTGGGCAGC commaggge ceregeatha gerereceta 201
- GAGGGAGAGA ACATCCTCAC ACCCGAAGCA TGTAGGAGTG TGGGCTTCGT AATGIGGITC CTCTTCGACC CCCTCCTCCG ACGIATGIGG AGAGICTACG ACTAIGICTG GCGIGCGGIC CICCCICTCT CGCACGCCAG TGCATACACC TCTCAGATGC TGATACAGAC TTACACCAAG GAGAAGCTGG GGGAGGAGGC 301
- AAGTCAGGAG GAACCGGAGG TGGAGGTCCG TCGGGAGTGA CGGTCATTC AGGTTCATAG TGAGATACCC TTCAGGACCC TAAACTTGTT TTAGACGATG TTCAGTCCTC AATCTGCTAC ATTTGAACAA AAGTCCTGGG ACCTCCAGGC AGCCCTCACT GCCAGTAAAG TCCAAGTATC ACTCTATGGG CTTGGCCTCC 401
- AAGGGGAATA ACTITIACCT TACTAACTCA CCTACTAACT CTTCGACAAA GGCACGCACT AGGAGTGGGG GGAGCTGACG AAGACCCTCC TTCTGGGAGG GGATGATIGA GAAGCIGITT CCGIGCGIGA ICCICACCCC CCICGACIGC TICCCCITIAI IGAAAAIGGA AIGAITGAGI 501
 - GGTTCCCCCG AGGCGGATGG ACGGGCCGGC GGGCCTATAG GTCACCTGGT TGGACCTAGG TCTCGTCGAC GACCTCCTCG ACCCAGGGAA ACGGAGGAAA TOCCCGGCCG CCCGGATATC CAGTGGACCA ACCTGGATCC AGAGCAGCTG CTGGAGGAGC TGGGTCCCTT TGCCTCCTT CCAAGGGGGC 601
- CCTAGTGCCC TOTGITCOGT GICCACCOGG ICOGGAIGCA COCCGCOGG ACAGACGIGG GACTACIGGA GGIGACGGGI GGAICACGGG CCACTGCCCA CTGATGACCT CAGGTGGGCC AGGCCTACGT GGGGGGGCCC TGTCTGCACC AGACAAGGCA CCCTCGACGA GGGAGCTGCT GAGGGCTTCC CTCCCGAAGG 701
 - TCCTTAACGA AGGAATTGCT CCAACCATCA CAGCAGGCAG GGTCCCAATG TGGCTCACGA GCTGAGTGGG GGCTGCCATG GCTTCTCCCA CAAATTCATG CACTGGCAGG GGTTGGTAGT GTCGTCCGTC CGAGGGTTAC ACCGAGTGCT CGACTCACCC CCGACGGTAC CGAAGAGGGT GTTTAAGTAC 801
- CGACCCTCCG TACCGGTCTC TGGGGGTTCC TCTCGACGAC TCCCGTCTCC GGGACGTCTC GTGGAAGAAC GACTACTCAG GGGCGGTCGA CATGCTCGTA cccgccagcr gracgagcar CTGATGAGTC GCTGGGAGGC ATGGCCAGAG ACCCCCAAGG AGAGCTGCTG AGGGCAGAGG CCCTGCAGAG CACCTTCTTG 901

FIG. 11A

CTTACAGCCA

- CTTTGTGCAG CTGGCCCAGG AAGGEEECEAE TGATAGTETG TGTAETGTAA EGGAEETEAE TECTEGTEEG GTEGTGTEAE GATGTTEGGA EEGTEGEEGE GAAACAEGTE GAEEGGGTEE TICCGGGGTG ACIAICAGAC ACATGACATT GGCTGGAGTG AGGAGCAGGC CAGCACAGTG CTACAAGCCT GGCAGCGGCG 1001
- TOCCAGOAGA TOCATGOOTT CTOCTOCACO ACCOTGGATA ACATOCTGCA TGOGTTOTOT GAAGTCAGTG CTGCCGTGT TCCGGGACGG ACTCTTGCGA AGGGTCGTCT AGGTACGGAA GAGGAGGTGG TGGGACCTAT TGTAGGACGT ACGCAAGAGA CTTCAGTCAC GACGGGCACA AGGCCCTGOĆ 1101
- GGTGGGAGGC TATCTGCTCA TGCTGGGCTA TGCCTGTGTG ACCATGCTGC GGTGGGACTG CGCCCAGTCC CAGGGTTCCG TGGGCCTTGC CGGGGTACTG CCACCTCCG ATAGACGAGT ACGACGGAT ACGGACACAC TGGTACGACG CCACCCTGAC GCGGGTCAGG GTCCCAAGGC ACCCGGAACG GCCCCATGAC 1201
- GACCACCGGG ACCGCCACCG GAGTCCGGAA CCCGAGACAC GGGACGAGCC GTAGTGGAAG TTACGACGGT GATGGGTCCA CGACGGGAAG AACCGAGACC CATCACCITC AATGCTGCCA CTACCCAGGT GCTGCCCTTC TTGGCTCTGG CTGGTGGCCC TGGCGGTGGC CTCAGGCCTT GGGCTCTGTG CCCTGCTCGG 1301
- GECGAGTGTC TGCAGCGCAC CTTAGCCGCA CCTACTGCAT AAGGACGACC GCGTACGGAA GTGTCTCCGA GACGGACCGT GGGGAGAGGT CCTCGCGTAC CCGCTCACAG ACGTCGCGTG GGAGCGCATG GAATCGGCGT GGATGACGTA ITCCTGCTGG CGCATGCCTT CACAGAGGCT CTGCCTGGCA CCCCTCTCCA 1401
 - CCCGTGGTCA CAGCATGAGT GTAGGTAGTT GTTGTACCGG CGGAAGGAGT ACCGACGGGA GCAAGGGTAG GGACGCGACG CTCGGAAGAG GAATGTCGGT GGGCACCAGT GTGGTACTCA CATCCATCAA CAACATGGCC GCCTTCCTCA TGGCTGCCCT CGTTCCCATC CCTGCGCTGC GAGCCTTCTC 1501
- GBACCIACGG CGGCGCCACT GCAGGGCCT TGATGTGCTC TGCTGCTTCT CCAGTCCCTG CTCTGCTCAG GTGATTCAGA TCCTGCCCCA AGGAGTOGGA CCTGGATGCC GCCGCGGTGA CGGTCGCGGA ACTACACGAG ACGACGAAGA GGTCAGGGAC GAGACGAGTC CACTAAGTCT AGGACGGGGT TCCTCAGCCT 1601
 - GGAGCTGGGG GACGGGACAG TACCAGTGGG CATTGCCCAC CTCACTGCCA CAGTTCAAGC CTTTACCCAC TGTGAAGCCA GCAGCCAGCA TGTGGTCACC CCTCGACCCC CTGCCCTGTC ATGGTCACCC GTAACGGGTG GAGTGACGGT GTCAAGTTCG GAAATGGGTG ACACTTCGGT CGTCGGTCGT ACACCAGTGG GGAGCTGGGG 1701
 - ATCCTGECTE ECCAAGECEA CETGGTGEE CEACETTETG ACCEACTGGG ETETGAGETE TTEAGECETG GAGGGTECAE AEGGGACETT ETAGGECAGG IAGGACGGAG GGGTTCGGGT GGACCACGGG GGTGGAGAC TGGGTGACCC GAGACTCGAG AAGTCGGGAC CTCCCAGGTG TGCCCTGGAA GATCCGGTCC 1801
 - TICCETCIIC CGICGGACGI ICAGGGACGG GACACGGGCG ACCTIAGAAC GGGTAAAGCG GGGCCTIAAG GACGICGGGC CCCCIAGGIG CCCGGAATTC CTGCAGCCCG GGGGATCCAC CCCATTTCGC AAGGCAGAAG GCAGCCTGCA AGTCCCTGCC CTGTGCCCGC TGGAATCTTG AGGAGGAGAC rccrcrcrg 1901
 - ATCAAGATCT CGCCGGCGGT GGCGCCACCT CGAGGTCGAA AACAAGGGAA ATCACTCCCA ATTAACGCGC GAACCCATAG AA Ţ TAGITCIAGA GCGGCCGCCA CCGCGGIGGA GCTCCAGCTT TTGITCCCTT TAGIGAGGGI TAATTGCGCG CTTGGGIATC (2001

FIG. 11B